NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of hybrid procedure for interim management of hypoplastic left heart syndrome (HLHS) in neonates

The hybrid procedure is performed on babies born with hypoplastic left heart syndrome. It consists of two or three different procedures which have the overall aim of establishing blood flow to and from the left side of the heart. The hybrid procedure is performed soon after birth, in order to delay the time of complex open heart surgery (the Norwood operation) until the baby is older and better able to withstand the surgery. The hybrid procedure involves both surgery, in which bands are placed around the branches of the pulmonary artery, and catheterisation techniques, in which stents (metal mesh tubes) are inserted to keep the ductus arteriosus open.

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in June 2007.

Procedure name

- Hybrid procedure for interim management of hypoplastic left heart syndrome in newborns

Specialty societies

- British Paediatric Cardiac Association
- Paediatric Intensive Care Society
- Royal College of Paediatrics and Child Health
- Society for Cardiothoracic Surgery in Great Britain and Ireland

- British Cardiovascular Intervention Society

Description

Indications

Hypoplastic left heart syndrome (HPLS)

HPLS is a combination of congenital abnormalities of the left side of the heart, characterised by a left ventricular outflow tract dysfunction with resulting underdeveloped left ventricle and aorta. Other abnormalities include absent, hypoplastic or blocked aortic and mitral valves and atrial septal defect (ASD, an abnormal communication between the left and right atria). The effect of these abnormalities is that oxygenated blood cannot enter the heart. Without surgical intervention the condition is fatal in the first 2 weeks of life.

Diagnosis of HLSS is often made at the routine screening ultrasound performed at about 20 weeks of pregnancy. Some babies will present in the first few days of life with bluish discoloration of the skin (cyanosis), rapid breathing (hyperpnoea) and cardiac failure. It is the most common cause of cardiac abnormality-related death in the first week of life.

Current treatment and alternatives

Immediately after birth a prostaglandin infusion is started to keep the Ductus Arteriosus open and investigation is undertaken to establish the severity of HLHS. For babies born with an adequate biventricular heart and aortic valve disease, postnatal balloon valvuloplasty is the initial preferred option to encourage remodelling and growth of the left ventricle. Further balloon valvuloplasty is often required with later valve replacement.

Babies born with HLHS are assessed for the suitability for staged reconstructive surgery. The option of heart transplantation is not currently a reality for most babies delivered in the UK.

Staged reconstruction
Staged reconstruction for HLHS requires up to three operations over three or more years and involves complex high risk open-heart surgery. The first stage, known as the Norwood procedure, is usually performed in the first one or two weeks of life while the ductus arteriosus is still open. It involves attaching the pulmonary artery to the aorta, inserting a synthetic shunt between the pulmonary artery and the right ventricle or the aorta and finally an atrial septectomy. This long complex open heart operation carries a high risk of intraoperative and post operative mortality. A number of babies die within the first few days or months or life despite successful surgery due to the extent of secondary aortic and myocardial disease or from persistent pulmonary hypertension.

As the child grows a more permanent blood supply to the lungs is required. Between 3 to 9 months of age either a Cavo Pulmonary Shunt (also known as

a Glenn Shunt) or a Hemi-Fontan procedure is performed. This surgery carries fewer risks than the first stage operation and involves connecting the Superior Vena Cava to the pulmonary artery and removal of the Gore-Tex shunt.

The final surgical operation of staged reconstruction is the Fontan procedure which is performed when the child starts to shows symptoms of increased breathlessness and slowing growth. Using one of two methods (baffle or synthetic conduit) the inferior vena cava is connected to the pulmonary artery thereby ensuring all blood returning from the body flows directly to the lungs.

Currently, over 80% of neonates who undergo stage 1 palliation (Norwood procedure) for HLHS in England survive to 30-days, and over 60% to one year. Post-operative survival after stage 2 (hemi-Fontan or bidirectional Glenn procedure) and stage 3 (Fontan procedure) surgery for HLHS is currently greater than 95% (for each procedure). Some children who survive staged reconstruction will reach adulthood in good health but some may need other cardiac procedures or require a heart transplant at a later stage.

What the procedure involves

The hybrid procedure combines surgical and endovascular techniques and is performed under general anaesthesia. The procedure is performed as soon as possible after birth. A median sternotomy is performed and bands are placed at the origins of the left and right pulmonary branch arteries. A guide wire is inserted percutaneously into the aorta and a self-expanding stent is advanced over the guide wire into the ductus arteriosus. A balloon-deployable stent may also be used. The stent is deployed to keep the ductus arteriosus patent and serve as a channel between the aorta and the pulmonary artery. More than one stent may be used and the pulmonary artery bands may be adjusted if necessary.

If the blood flow across the atrial septum is restricted, a balloon atrial septostomy is performed. A balloon-catheter is guided to the heart, following percutaneous insertion into the blood vessels of the forearm or thigh. The balloon is inflated to widen the atrial septal defect. If this procedure is not technically possible or is unsuccessful, a hole in the atrial wall may be created surgically (atrial septostomy).

Together, the above procedures of pulmonary branch banding, ductus arteriosus stenting and atrial septostomy establish blood flow from the left side of the heart to the right side. Unlike the Norwood procedure; they do not require cardiopulmonary bypass.

The purpose of the hybrid procedure is to delay the need for complex open heart surgery until the patient is older. A subsequent procedure which combines the first 2 conventional operations is performed at 12 to 25 weeks of age. This procedure consists of removal of the ductus arteriosus stent, surgical reconstruction of the aorta and establishment of bidirectional cavopulmonary connection.

Efficacy

The Specialist Advisers stated that the key efficacy outcomes include survival to second- and third-stage surgery, long-term survival, freedom from neurological damage, length of stay in intensive care, length of hospital stay, mortality and complication rates compared with the conventional surgical procedure, and progression to Fontan completion.

Progression to stage 2 procedure
In a case series of 58 patients, 54 progressed to a stage 2 procedure (biventricular repair, univentricular repair or cardiac transplant). Of these patients, 46 survived the stage 2 procedure and 2 were waiting for procedures at the time of publication.[1] Seven additional late procedures (stent placements) were reported in this case series, for recurrent aortic coarctation, left ventricle stenosis, stenotic bidirectional Glenn anastomosis and left bronchus stenosis.

In one case series, 62% of patients (18/29) went on to have a stage 2 operation, and 3 patients were awaiting one at the time of publication.[2]

In another case series of 40 patients, 88% (15/17) of patients who underwent a hybrid procedure were discharged home and had adequate growth and pulmonary circulation.[3] In this case series, 10 patients underwent a successful heart transplant at a median of 42 days after the hybrid procedure.

One case series reported outcomes for 5 high-risk patients who underwent the hybrid procedure, and 17 standard- and high-risk patients who underwent the conventional Norwood procedure.[4] All patients survived the Hybrid procedure however two died before stage 2 procedures were performed. Of the remaining patients, 1 had a successful heart transplant and 2 were awaiting stage 2 procedures at the time of publication. Of 11 patients who survived the Norwood procedure (65%), 9 had successful stage 2 operations and 2 were awaiting procedures at the time of publication.

In a case series of 14 patients, 8 (57%) progressed to stage 2 procedures (stent removal, aortic arch reconstruction and cavopulmonary shunt), 6 of whom survived these procedures.[5]

Late mortality
One case series of 29 patients reported 4 deaths relating to stage 2 procedures and 1 late death of a patient awaiting heart transplant.[2] Another case series of 17 patients reported 4 late deaths occurring up to 115 days after the procedure[3].

In a case series of 5 patients who underwent the hybrid procedure and 17 patients who underwent the Norwood procedure, 2 patients who survived the hybrid procedure and 1 patient who survived the Norwood procedure died before undergoing a stage-2 procedure.[4]

In a case series of 14 patients, there were 2 deaths in the period between this and the stage 2 surgery.[5] Of the 8 patients who underwent stage 2 surgery, 2 died during the procedure and 1 died later at home from a sudden infection.[5]

Safety

The Specialist Advisers stated that theoretical safety events include death, brain damage, bleeding, infection, heart failure, damage to pulmonary arteries, stent migration, stent stenosis, stent thrombosis, migration of the pulmonary artery bands after band dilation, and duct perforation.

Mortality
The case series of 58 patients reported 30-day mortality of 3% (2/58). One baby died from ductal stenting and one died after bilateral pulmonary artery banding.[1] The overall mortality in the study period was 10/58 (17%) (follow-up period not reported).

One case series of 29 patients reported 5 hospital deaths (17%) after the hybrid procedure and 3 deaths in the period between the hybrid procedure and stage 2 procedures.[2]

A case series of 17 patients who underwent the hybrid procedure reported 1 procedural death (6%) during atrial septostomy.[3]

In the case series of 5 patients who underwent the hybrid procedure and 17 patients who underwent the Norwood procedure, there were no procedure-related deaths in the former group and 6 (35%) in the latter group.[4]

In a case series of 14 patients, there were 3 hospital deaths (21%) during the hybrid procedure.[5]

Complications
In the case series of 29 patients, 2 required prolonged hospital stay, because of emergent atrial septoplasty and atrial arrhythmias.[2]

One study reported 6 complications relating to banding of the pulmonary artery in 17 patients who underwent the hybrid procedure. These were due to use of an oversized device (n = 2), acute device occlusion (n = 2) and unbalanced atrio–ventricular septal defect (which led to the death of the patient).[3]

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to the hybrid procedure (bilateral branch pulmonary artery banding with ductus arteriosus stenting) for interim management of HLHS in newborns. Searches were conducted via the following databases, covering the period

from their commencement to 6th June, 2007: Medline, PreMedline, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches. (See Appendix C for details of search strategy.)

The following selection criteria (Table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Neonates with hypoplastic left heart syndrome
Intervention/test	Hybrid procedure for interim management of hypoplastic left heart syndrome in newborns
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on five case series.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (Table 2) have been listed in Appendix A.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B details the recommendations made in each piece of guidance listed below.

Interventional procedures

‘Balloon dilatation of systemic to pulmonary arterial shunts in children’. NICE interventional procedures guidance 77 (2004). Available from: http://guidance.nice.org.uk/IPG77 .

‘Balloon dilatation with or without stenting for pulmonary artery or non-valvar right ventricular outflow tract obstruction in children’. NICE interventional procedures guidance 76 (2004). Available from: http://guidance.nice.org.uk/IPG76 .

‘Balloon angioplasty of pulmonary vein stenosis in infants’. NICE interventional procedures guidance 75 (2004). Available from: http://guidance.nice.org.uk/IPG75 .

‘Endovascular atrial septostomy’. NICE interventional procedures guidance 86 (2004). Available from: http://guidance.nice.org.uk/IPG86 .

‘Endovascular closure of patent ductus arteriosus’. NICE interventional procedures guidance 97 (2004). Available from: http://guidance.nice.org.uk/IPG97 .

‘Percutaneous fetal balloon valvuloplasty for aortic stenosis’. NICE interventional procedures guidance 175 (2006). Available from: http://guidance.nice.org.uk/IPG175

Table 2 Summary of key efficacy and safety findings on hybrid procedure for interim management of hypoplastic left heart syndrome in neonates

Abbreviations used: CPB, cardiopulmonary bypass; DA, ductus arteriosus; HLHS, hypoplastic left heart syndrome; PA, pulmonary artery;			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Akintürk et al (2007)[1] Case series Germany June 1998 – March 2006 n = 58 Inclusion criteria: 36 neonates with typical HLHS, 22 neonates with hypoplastic left heart complex (left ventricular obstructive or hypoplastic lesions with duct-dependent systemic flow). Age: 'newborns' (further details not reported) Technique: surgical bilateral PA banding followed by percutaneous DA stenting. (Early in the series, stenting was performed before banding was carried out but procedures were subsequently reversed after stent dislocation in 2 neonates). Balloon-expandable and self-expandable stents were used. Balloon dilation of the atrial septum was performed when indicated. Stage 2 operations: Patients were scheduled to receive either a univentricular repair with aortic reconstruction and bilateral cavopulmonary connection which was the final step of the Norwood pathway (n = 28), or a biventricular repair (n = 19). Follow-up: Not stated Conflict of interest: None stated	**Outcomes after hybrid procedure (n = 58)** • 51 patients (88%) were discharged home. • 13 patients (22%) required a second stent. • 11 patients (19%) required balloon atrial septal dilatation 4–14 weeks after the initial procedure • 5 patients (9%) had stenting of the interatrial septum in addition to PA banding and DA stenting • 3 patients (5%) were treated with stenting within a significant coarctation **Progression to stage 2 operation (n = 54)** *Biventricular repair* (n = 18) • All patients survived and were discharged home • 1 patient "died suddenly, months after the procedure" *Univentricular repair* (median age: 4.8 months; n = 27) • 24 patients survived (89%) • 11 went on to have total cavopulmonary connection without mortality at median age of 3.1 years • 5 went on to have heart transplant or bidirectional cavopulmonary connection • 3 patients died (11%) (1 during surgery; 1 from lymphangiectasis 5 weeks after the procedure; 1 while awaiting heart transplant) *Cardiac transplant* (n = 9) • 6 patients had heart transplant after the hybrid procedure (5 were discharged home; 1 died after the procedure) • 3 patients died while waiting for transplant 2 patients were awaiting stage 2 operations at time of publication. **Additional late procedures:** Stent placement (n = 7) for recurrent aortic coarctation, stenosis of left ventricle, stenotic	**30-day mortality (hybrid procedure): 2/58 (3%)** 1 patient died from ductal stenting 1 patient died after bilateral banding **Overall mortality: 10/58 (17%)** **Serious neurological complications: 3/58 (5%)**	

Abbreviations used: CPB, cardiopulmonary bypass; DA, ductus arteriosus; HLHS, hypoplastic left heart syndrome; PA, pulmonary artery;			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Galantowicz & Cheatham (2005)[2] Case series Ohio, USA Aug 2001 – Dec 2004 n = 29 Inclusion criteria: neonates with HLHS Age range: 1–92 days (mean: 11 days) Technique: - 2 patients had entirely transcatheter techniques (balloon-expandable DA stent, balloon atrial septostomy, placement of PA flow restrictors) - 3 patients had balloon-expandable stent, atrial septostomy if needed and within 24 hours went to operating room for PA banding without CPB - 7 patients had surgical PA banding in operating room, followed by DA stenting and atrial septostomy in catheterisation lab - 17 patients had hybrid procedure performed in cath lab or operating room: PA banding and self-expandable DA stenting. Treatment of atrial septal defect performed in cath lab in a separate procedure. **Patient group 1 (n = 10):** first patients who were treated prior to interstage monitoring protocol (close monitoring with weekly cardiology assessment after discharge home) and representing a significant learning curve **Patient group 2 (n = 19):** subsequent patients treated more uniformly and with interstage monitoring after discharge Follow-up: Not stated Conflict of interest: None stated	**Progression to stage 2 operation: 18/29 (62%)** • Patient group 1: 4/10 (40%) • Patient group 2: 14/19 (74%) • 3 patients were awaiting stage 2 operations at the time of publication **Interstage mortality: 3/29 (10%)** All in patient group 1 Causes: avulsion of the pulmonary veins during conventional balloon septostomy (1), late detected coarctation (1), unknown cause (1) **Peri-operative mortality (stage 2 procedure): 4/29 (14%)** • Patient group 1: 2/10 (20%) Cause: ventricular dysfunction secondary to coarctation (2) • Patient group 2: 2/19 (11%) Causes: unknown cause 3 days postoperatively (1), pneumonia 2 weeks postoperatively (1) **Late mortality** • 1 late death in a patient awaiting heart transplant for ventricular failure 14 months after stage 2 operation	**Hospital mortality (hybrid): 5/29 (17%)** • Patient group 1: 3/10 (30%) Causes: The first 2 patients in the series who had total transcatheter palliation died from procedure-related organ damage, which led to abandonment of the procedure; arrhythmia after balloon septostomy (1) • Patient group 2: 2/19 (11%) Causes: sepsis after congenital diaphragmatic hernia repair (1), arrhythmia after stent deployment in premature patient (1) **Morbidity** 2 patients had significant postoperative morbidity, requiring prolonged hospital stay (emergent atrial septoplasty, atrial arrythmias)	Mortality was high in the first 10 patients, whereas there were no procedural or interstage deaths in the latter patients. The authors highlighted that this reflects the significant learning curve associated with the procedure.

Abbreviations used: CPB, cardiopulmonary bypass; DA, ductus arteriosus; HLHS, hypoplastic left heart syndrome; PA, pulmonary artery;			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Chan et al (2006)[3] Colorado, USA Case series Jan 2000 – Oct 2004 **n = 40** (17 patients had 'complete palliation': DA stenting AND PA banding; 23 patients had DA stenting alone) Inclusion criteria: 34 patients with 'classic' HLHS, 6 patients with HLHS 'variants' (atrioventricular septal defect, Shore's complex with small left ventricle, or single ventricle). All patients were referred for cardiac transplant. Age range: 2–210 days (mean ± SD 50 ± 41 days) Age of 17 patients undergoing complete palliation: 48–131 days (mean ± SD 85 ± 41 days) Technique: DA stenting with self-expandable stent alone (n = 23) or in combination with PA banding and widening of the interatrial communication (n = 17) Follow-up: Until transplant or death (mean: 65 ± 65 days) Conflict of interest: None stated	15 of the 17 patients (88%) who underwent complete palliation were discharged home and had adequate growth and pulmonary circulation. **Progression to cardiac transplant (in patients who underwent complete palliation): 11/17 (65%)** • 11 patients survived to transplant but 1 patient with developmental delay did not undergo the transplant • 10 transplants were performed at a median of 42 days after complete palliation Pulmonary angiography 1 year after transplant showed no stenosis or distortion of the PAs **Late mortality: 4/17 (24%)** (occurring up to 115 days after the procedure) • Persistent pulmonary hypertension (2) • Unbalanced atrioventricular septal defect and progressive heart failure (1) • Reverse coarctation 3 months after PDA stenting (1)	**Mortality (in patients who underwent complete palliation): 1/17 (6%)** • 1 procedural death during atrial septostomy (embolism from PA band thrombosis) Complications relating to PA banding: 6/17 (35%) • oversized devices (2) • acute device occlusion (2) • unbalanced atrioventricular septal defect and progressive heart failure (1) • 1 complication not described Significant complications relating to PDA stenting: 9/40 (23%) • Bradycardia (3) • Hypotension (4) • Transient heart block (1) • Respiratory arrest with sedation (1) In addition, there were 3 late complications: coarctation of aorta at 1 month (2) and 3 months (1) after PDA stenting (patient died)	Authors state that complications were more common early in their experience reflecting the learning curve. **The mean age of patients undergoing complete palliation (hybrid procedure) (85 days) was older than in other studies.** Background: Prior to 2003, cardiac transplant was the only available treatment for HLHS at this centre. Patients received palliative prostaglandin infusion to maintain ductal patency and DA stenting was used if required. Additional DA banding and atrial septostomy or static balloon angioplasty were only performed if wait for transplant exceeded 4 months. Subsequent patients all underwent complete palliation.

Abbreviations used: CPB, cardiopulmonary bypass; DA, ductus arteriosus; HLHS, hypoplastic left heart syndrome; PA, pulmonary artery;

Study details	Key efficacy findings	Key safety findings	Comments
Lim et al (2006)[4] Case series Virginia, USA Nov 2002 – Feb 2005 n = 22 (10 standard-risk patients who underwent Norwood–Sano procedures; 7 high-risk patients who underwent Norwood–Sano procedures; 5 high-risk patients who underwent hybrid palliation) Population: neonates with HLHS. High-risk features: severe tricuspid insufficiency, severe right ventricular dysfunction, severely restricted or intact atrial septum, ascending aortic diameter ≤ 2 mm, late presentation, weight < 2 kg, or significant extracardiac issues Technique: Norwood–Sano procedure: conventional Norwood stage 1 operation with Sano medication (no further description provided) Hybrid procedure: Bilateral PA banding, ductal stenting, atrial septosomy Follow-up: Not stated Conflict of interest: None stated	**Progression to stage 2 procedure** 3 survivors of hybrid procedure: • 1 patient was successfully bridged to heart transplant 4 weeks postoperatively • 2 premature patients were awaiting stage 2 palliation at time of publication 11 survivors of Norwood–Sano procedure: • 9 patients successfully underwent stage 2 Glenn procedure • 2 patients were awaiting stage 2 operation at time of publication **Interstage mortality** • Hybrid procedure: 2/5 (40%) 1 patient had acute decompensation following a feeding with ememsis and died 5 weeks postoperatively. Cause of second death not reported. Norwood–Sano procedure: 1/11 (9.1%) (acute collapse at home)	**Operative mortality** • Hybrid procedure: 0/5 • Norwood–Sano procedure: Standard-risk patients: 1/10 (10%) High-risk patients: 5/7 (71%) **Mean intensive care stay** • Hybrid procedure: 19 days (± 6 days) • Norwood–Sano procedure: Standard-risk patients: 10 days (± 4 days) High-risk patients: 14 days (± 5 days)	This study reports only short-term follow-up outcomes. Patients undergoing the hybrid procedure had high-risk indications, unlike the other studies in Table 2.

Abbreviations used: CPB, cardiopulmonary bypass; DA, ductus arteriosus; HLHS, hypoplastic left heart syndrome; PA, pulmonary artery;

Study details	Key efficacy findings	Key safety findings	Comments
Bacha et al (2006)[5] Case series Illinois, USA Oct 2003 – June 2005 n = 14 Inclusion criteria: 11 patients with HLHS, 3 patients with interruption of the aortic arch Median age: 5.7 days (range 1–17) Technique: Bilateral PA banding performed via a median sternotomy. DA stenting performed with a self-expandable stent. Self-expandable stent placed to enlarge atrial communication if required. Stage 2 procedure: stent removal, aortic arch reconstruction, cavopulmonary shunt Follow-up: Not stated (age of patients at follow-up ranged from 4 weeks to 19 months) Conflict of interest: None stated	**Progression to stage 2 procedure: 8/14 (57%)** **Survival of stage 2 procedure: 6/8 (75%)** **Survival at follow-up: 5/6** Patients ranged from 5 to 19 months of age at follow-up. 1 patient was awaiting a stage 2 procedure at the time of publication. **Interstage mortality: 2/11 (18%)** • 1 patient died suddenly 8 days after discharge (27 days post-operatively); autopsy showed an opening into the transverse arch with ductal tissue surrounding that opening • 1 patient died immediately before stage 2 operation, from subacute occlusion (stent migration), aged 5 months **Peri-operative mortality (stage 2 procedure): 2/8 (25%)** • 1 patient died from heparin -induced thrombocytopenia and thrombosis • 1 patient died from low cardiac output **Late mortality: 1/6** 1 patient died suddenly at home from infection, aged 8 months	**Hospital mortality: 3/14 (21%)** • Cardiac arrest during procedure and subsequent sepsis at 8 weeks of age • Stent dislodgement on day of discharge • Cardiac arrest 6 hours after an uneventful procedure in a severely dysmorphic patient	

Abbreviations used: CPB, cardiopulmonary bypass; DA, ductus arteriosus; HLHS, hypoplastic left heart syndrome; PA, pulmonary artery;			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Gibbs et al (1993)[6] Case series UK Study period: Not stated n = 4 Inclusion criteria: neonates with HLHS Ages: 34, 22, 19 and 11 days Technique: 3 patients underwent PA banding via median sternotomy followed by DA stenting (and atrial septectomy in 2 patients). 1 patient underwent DA stenting and balloon atrial septostomy followed by PA banding. Follow-up: Not stated (age of patients at follow-up ranged from 4 weeks to 19 months) Conflict of interest: None stated	1 patient was discharged home 2 weeks after the procedure and was well at follow-up at age 16 weeks. 1 patient was haemodynamically stable and steadily improving, but remained in hospital 5 weeks after the procedure (at time of publication) because he required diuretic therapy due to high pulmonary blood flow.	**Mortality** All patients survived the immediate postoperative period. 2 patients (50%) could not be weaned from ventilation after the procedure because of ventricular failure and respiratory infection and died 2 weeks later.	**Follow-up to stage 2 procedures was not reported**

Validity and generalisability of the studies

- Studies were included in this review if procedures included stenting of the ductus arteriosus *and* banding of the pulmonary arteries (with or without atrial septostomy or other methods of enlarging atrial communication) in the neonatal period. Studies were not included where only one of these techniques was employed or if a hybrid procedure was performed in a non-primary fashion (i.e. after previous cardiac surgery).

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.
John Gibbs, Dr Robin Martin, Mr David Anderson, Dr John Thomson, Dr Shane Tibby, Mr David Barron, Dr Aung Soe

- All Specialist Advisers stated that only a few specialists perform the procedure, and that the potential impact on the NHS is minor.
- The procedure should be carried out by an experienced paediatric cardiac surgeon and an experienced interventional paediatric cardiologist, and should only be carried in centres specialising in the management of complex congenital heart disease and by surgeons who are competent in performing the standard Norwood operation. The procedure requires a specialised cardiac catheter laboratory, where surgical and catheterisation techniques can be carried out at the same time.
- Selection of patients is controversial; one Specialist Adviser commented that the place of the procedure was uncertain and it may be best reserved for high-risk surgical cases.
- There is uncertainty about the efficacy of the procedure because only small numbers of patients have been treated. There is also uncertainty about whether any benefit gained by the procedure outweighs the potential risk associated with a stage 2 operation that could be more complex than the standard stage 2 operation. The procedure may shift mortality from the neonatal period to the infant period.
- The short-term efficacy of the procedure for balancing systemic and pulmonary circulation is established, but long-term efficacy, specifically survival compared with the standard Norwood protocol, is not yet established.
- The safety and efficacy of the procedure should be considered in the contexts of the high-risk nature of the condition and the surgical alternative.

Issues for consideration by IPAC

- No data on long-term outcomes are reported (i.e. survival to third stage procedures and beyond Fontan completion).

- Only one small observational study compared patients undergoing the hybrid procedure with those undergoing the conventional surgical procedure. No studies compared long-term outcomes of each procedure.

References

1 Akintürk H, Michel-Behnke I, Valeske K et al. (2007) Hybrid transcatheter-surgical palliation – Basis for univentricular or biventricular repair: The Giessen experience. *Pediatric Cardiology* 28: 79–87.

2 Galantowicz M, Cheatham JP. (2005) Lessons learned from the development of a new hybrid strategy for the management of hypoplastic left heart syndrome.[republished from *Pediatr. Cardiol.* 2005 26(2):190–9; PMID: 15906023]. *Pediatric Cardiology* 26: 190–199.

3 Chan K-C, Mashburn C, Boucek MM. (2006) Initial transcatheter palliation of hypoplastic left heart syndrome. *Catheterization & Cardiovascular Interventions* 68: 719–726.

4 Lim DS, Peeler BB, Matherne GP et al. (2006) Risk-stratified approach to hybrid transcatheter-surgical palliation of hypoplastic left heart syndrome. *Pediatric Cardiology* 27: 91–95.

5 Bacha EA, Daves S, Hardin J et al. (2006) Single-ventricle palliation for high-risk neonates: the emergence of an alternative hybrid stage I strategy. *Journal of Thoracic & Cardiovascular Surgery* 131: 163–171.

6 Gibbs JL, Wren C, Watterson KG et al. (1993) Stenting of the arterial duct combined with banding of the pulmonary arteries and atrial septectomy or septostomy: a new approach to palliation for the hypoplastic left heart syndrome.[see comment]. *British Heart Journal* 69: 551-555.

7 Bove EL, Lloyd, TR. (1996) Staged Reconstruction for Hypoplastic Left Heart Syndrome: Contemporary Results. *Annals of Surgery*. 224: 387–395.

8 Tweddell JS, Hoffman GM, Mussatto KA et al. (2002) Improved Survival of Patients Undergoing Palliation of Hypoplastic Left Heart Syndrome: Lessons Learned From 115 Consecutive Patients. *Circulation*. 106: 82–89.

9 Douglas WI, Goldberg CS, Mosca,RS, et al. (1999) Hemi-Fontan procedure for hypoplastic left heart syndrome: outcome and suitability for Fontan. *Annals of Thoracic Surgery* 68: 1361–1367.

10 Bove EL. (1998) Current Status of Staged Reconstruction for Hypoplastic Left Heart Syndrome. *Journal of Pediatric Cardiology* 19: 308–315

Mahle WT, Spray TL, Wernovsky G et al (2000) Survival after reconstructive surgery for hypoplastic left heart syndrome. A 15-year experience from a single institution. *Circulation* 102: 136–141.

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Appendix A: Additional papers on hybrid procedure for interim management of hypoplastic left heart syndrome in neonates not included in summary Table 2

The following table outlines studies that are considered potentially relevant to the overview but were not included in the main data extraction table (Table 2). It is by no means an exhaustive list of potentially relevant studies.

Article title	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in Table 2
Akintuerk H, Michel-Behnke I, Valeske K et al. (2002) Stenting of the arterial duct and banding of the pulmonary arteries: basis for combined Norwood stage I and II repair in hypoplastic left heart. *Circulation* 105: 1099–1103.	n = 11 Follow-up: not stated	No deaths during hybrid procedure. 2 patients underwent heart transplant. 8 patients had stage 2 procedures; 2 died.	More recent study from same centre (reporting on the same patients) included in Table 2.
Atrip J, Campbell D, Ivy D et al. (2006) Birth weight and complexity are significant factors for the management of hypoplastic left heat syndrome. Annals of Thoracic Surgery 82: 1252-9.	n = 69 (7 patients underwent catheter-based or surgical-hybrid procedures) Follow-up: Not stated	Focus of the study is on risk factors influencing the decision between transplant and Norwood procedure. Results are not reported separately for patients who underwent hybrid procedures and those who didn't.	
Michel-Behnke I, Akintuerk H, Marquardt I et al. (2003) Stenting of the ductus arteriosus and banding of the pulmonary arteries: basis for various surgical strategies in newborns with multiple left heart obstructive lesions. *Heart* 89: 645–650.	n = 20 Follow-up: not stated	1 patient died from PDA stenting;1 patient died from PA banding during hybrid procedure. 2 patients underwent heart transplant; 2 died awaiting transplant. 10 patients had stage 2 procedures, 1 died.	More recent study from same centre (reporting on the same patients) included in Table 2.

Appendix B: Related published NICE guidance for hybrid procedure for interim management of hypoplastic left heart syndrome in neonates

Guidance programme	Recommendation
Interventional procedures	**IPG077 Balloon dilatation of systemic to pulmonary arterial shunts in children** 1.1 Current evidence on the safety and efficacy of balloon dilatation of systemic to pulmonary arterial shunts in children appears adequate to support the use of this procedure, provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 The procedure should only be undertaken in specialist paediatric cardiology units. 1.3 The Department of Health runs the UK Central Cardiac Audit Database (UKCCAD) and clinicians are encouraged to enter all patients into this database (www.ccad.org.uk). **IPG076 Balloon dilatation with or without stenting for pulmonary artery or non-valvar right ventricular outflow tract obstruction in children** 1.1 Current evidence on the safety and efficacy of balloon dilatation with or without stenting for pulmonary artery or non-valvar right ventricular outflow tract obstruction in children appears adequate to support the use of this procedure, provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 The procedure should only be undertaken in specialist paediatric cardiology units. 1.3 The Department of Health runs the UK Central Cardiac Audit Database (UKCCAD) and clinicians are encouraged to enter all patients into this database (www.ccad.org.uk). **IPG075 Balloon angioplasty of pulmonary vein stenosis in infants** 1.1 Current evidence on the safety and efficacy of balloon angioplasty of pulmonary vein stenosis in infants does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research. The available evidence suggests

	that the procedure is not efficacious. However, there are no special concerns about the safety of the procedure, especially in the context of very ill infants for whom it is used. 1.2 Clinicians wishing to undertake balloon angioplasty of pulmonary vein stenosis in infants should take the following actions: • Inform the clinical governance leads in their Trusts. • Ensure that the parents of patients understand that the limited available evidence indicates a lack of efficacy. Parents should be given clear written information. Use of the Institute's Information for the Public is recommended. • Audit and review clinical outcomes of all patients having balloon angioplasty of pulmonary vein stenosis in infancy. 1.3 This procedure should only be offered to gravely ill infants with a very poor prognosis, and in the setting of a specialist paediatric cardiology unit. 1.4 The Department of Health runs the UK Central Cardiac Audit Database (UKCCAD) and clinicians are encouraged to enter all patients onto this database (www.ccad.org.uk). 1.5 Publication of safety and efficacy outcomes will be useful in reducing the current uncertainty. The Institute may review the procedure upon publication of further evidence. **IPG086 Endovascular atrial septostomy** 1.1 Current evidence on the safety and efficacy of endovascular atrial septostomy appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance. 1.2 Endovascular atrial septostomy should be undertaken only by specialist paediatric cardiology teams. 1.3 The Department of Health runs the UK Central Cardiac Audit Database (UKCCAD) and clinicians are encouraged to enter all patients onto this database (www.ccad.org.uk). **IPG175 Percutaneous fetal balloon valvuloplasty for aortic stenosis** 1.1 Current evidence on the safety and efficacy of percutaneous fetal balloon valvuloplasty for aortic stenosis does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research.

	1.2 Clinicians wishing to undertake percutaneous fetal balloon valvuloplasty for aortic stenosis should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that parents understand the uncertainty about the procedure's safety and efficacy. Clinicians should provide parents with clear written information, and with counselling and support both before and after the procedure. In addition, use of the Institute's Information for the public is recommended (available from www.nice.org.uk/IPG175publicinfo). • Audit and review the clinical outcomes of percutaneous fetal balloon valvuloplasty for aortic stenosis. 1.3 This procedure should only be performed in centres specialising in invasive fetal medicine and in the context of a multidisciplinary team including a consultant in fetal medicine, a paediatric cardiologist, a neonatologist, a specialist midwife and a paediatric cardiac surgeon. 1.4 An intention-to-treat registry has been developed by the Association for European Paediatric Cardiology (www.aepc.org), and clinicians are encouraged to enter all cases into this registry. 1.5 Further publication on the criteria for patient selection will be useful. The Institute may review the procedure upon publication of further evidence.
Technology appraisals	None applicable
Clinical guidelines	None applicable
Public health	None applicable

Appendix C: Literature search for hybrid procedure for interim management of hypoplastic left heart syndrome in neonates

IP: 405 Hybrid procedure (bilateral branch pulmonary artery banding with ductus arteriosus stenting) for interim management of hypoplastic left heart syndrome in newborns		
Database	**Date searched**	**Version searched**
Cochrane Library	11/06/2007	Issue 2, 2007
CRD databases (DARE & HTA)	11/06/2007	Issue 2, 2007
Embase	12/06/2007	1980 to 2007 Week 20
Medline	12/06/2007	1950 to April Week 4 2007
Premedline	12/06/2007	June 11, 2007
CINAHL	12/06/2007	1982 to May Week 1 2007
British Library Inside Conferences	11/06/2007	1993 to date
NRR	11/06/2007	2007 – Issue 2
Controlled Trials Registry	11/06/2007	-

The following search strategy was used to identify papers in Medline. A similar strategy was used to identify papers in other databases.

1. exp Hypoplastic Left Heart Syndrome/
2. hypoplastic left heart$.tw.
3. HLHS.tw.
4. or/1-3
5. exp Pulmonary Artery/
6. (pulmon$ art$ adj3 band$).tw.
7. 5 or 6
8. exp Stents/
9. stent$.tw.
10. 8 or 9
11. exp Ductus Arteriosus/
12. (duct$ adj3 arter$).tw.
13. exp Ductus Arteriosus, Patent/
14. PDA.tw.
15. or/11-14
16. (hybrid adj3 (proced$ or stage$ or palliat$ or therap$)).tw.
17. (7 and (10 or 15)) or 16
18. 4 and 17